

WE CLAIM:

1. A DNA expression vector comprising:
 - i) a first DNA sequence comprising the coding sequence for one or more protein having a detectable signal;
 - ii) one or more 3' UTR sequence and one or more expression control sequence operatively associated with said coding sequence, and
 - iii) a heterologous instability sequence DNA inserted into said 3' UTR sequence comprising a second DNA sequence corresponding to one or more mRNA instability sequence derived from one or more naturally occurring genes.
2. The DNA expression vector according to claim 1, wherein said heterologous instability sequence DNA further comprises DNA corresponding to sequences that flank said mRNA instability sequence in the naturally occurring gene.
3. The DNA expression vector according to claim 1, wherein said heterologous instability sequence DNA is from about 10 to about 1500 nucleotides in length.
4. The DNA expression vector according to claim 2, wherein said heterologous instability sequence DNA comprises DNA corresponding to the whole, or a substantial part, of the 3' UTR from said naturally occurring genes.
5. The DNA expression vector according to claim 2, wherein said heterologous instability sequence DNA comprises DNA corresponding to one or more CRD from the coding region of said naturally occurring genes.
6. The DNA expression vector according to claim 1, wherein said one or more naturally occurring genes is selected from the group of: a gene encoding a cytokine, a gene encoding a chemokine, a gene encoding a nuclear transcription factor, a gene encoding an oxygenase, a proto-oncogene, an immediate early gene, a cell cycle controlling gene, and a gene involved in apoptosis.

7. The DNA expression vector according to claim 1, wherein said one or naturally occurring genes is selected from the group of: a gene encoding APP, VEGF, GM-CSF, c-fos, c-myc, c-jun, krox-20, nur-77, zif268, bcl-2, β -IFN, uPA, IL-1 α , IL-1 β , IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-13, TNF α , synl, β 2-AR, E-selectin, VCAM-1, ICAM-1, Gro- α , Gro- β , MIP-2 α , Gro- γ , MIP-2 β , MMP-1, MMP-2, collagenases, P-glycoproteins, MDR, MRPs, P_{yh1}, pfmdr, COXII, endothelial lipase, cholesterylester transfer protein, β -adrenergic receptor, MIP-1 α , MIP-1 β , MCP-1, MCP-2, nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor alpha, IFN γ inducible protein 10 kD, cyclophilin F, IL-10 receptor alpha, AUF1, tristetraproline, and ubiquitin specific protease 18.
8. A host cell comprising the DNA expression vector according to claim 1.
9. A stably transfected cell line comprising:
 - i) a DNA expression vector comprising a first DNA sequence encoding a first protein having a detectable signal, one or more 3' UTR sequence and one or more expression control sequence operatively associated with said first DNA sequence, and a heterologous instability sequence DNA inserted into said 3' UTR sequences, said instability sequence DNA comprising a second DNA sequence corresponding to one or more mRNA instability sequence derived from one or more naturally occurring genes; and
 - ii) a control DNA expression vector comprising a control DNA sequence encoding a second protein having a detectable signal, and one or more 3' UTR sequence and one or more expression control sequence operatively associated with said control DNA sequence.
10. A method of screening for one or more compound which affect mRNA stability comprising the steps of:
 - i) providing a DNA expression vector, which in the absence of a test compound is capable of expressing a protein having a detectable signal, wherein the mRNA which is transcribed from said expression vector and encodes said protein comprises at least one copy of a heterologous mRNA instability sequence;

(ii) contacting said DNA expression vector with at least one test compound under conditions whereby, in the absence of the test compound, said DNA expression system is capable of expressing said protein having a detectable signal;

(iii) measuring said detectable signal; and

(iv) comparing the measured detectable signal with a control,

wherein a decrease in the measured detectable signal compared to said control indicates a compound that decreases mRNA stability and an increase in the measured detectable signal compared to said control indicates a compound that increases mRNA stability.

11. The method according to claim 10, wherein said control comprises measuring the detectable signal from the DNA expression vector in the absence of said test compound.

12. The method according to claim 10, wherein said control comprises contacting a control expression vector capable of expressing a second protein having a second detectable signal with the test compound and measuring said second detectable signal.

13. The method according to claim 10, wherein said compounds are being screened for their ability to induce mRNA degradation, and wherein a decrease in the measured detectable signal compared to said control indicates a compound that induces mRNA degradation.

14. A method for comparing the extent of mRNA degradation induced by two or more compounds comprising the steps of:

(i) providing a DNA expression vector, which in the absence of a test compound is capable of expressing a protein having a detectable signal, wherein the mRNA which is transcribed from said expression vector and encodes said protein comprises at least one copy of a heterologous mRNA instability sequence;

(ii) contacting said DNA expression vector separately with two or more test compounds under conditions whereby, in the absence of the test compounds, said DNA expression system is capable of expressing said protein having a detectable signal;

(iii) measuring said detectable signal in the presence of each test compound; and

(iv)comparing the measured detectable signals; wherein a lower measured detectable signal indicates a greater extent of mRNA degradation.

15. An assay system for screening for compounds which destabilise mRNA comprising:

- (i) a DNA expression vector comprising a first DNA sequence encoding a first protein having a detectable signal, one or more 3' UTR sequence and one or more expression control sequence operatively associated with said DNA sequence, and a heterologous instability sequence DNA inserted into said 3' UTR sequence, said instability sequence DNA comprising a second DNA sequence corresponding to one or more mRNA instability sequence derived from one or more naturally occurring genes; and
- (ii) a control DNA expression vector comprising a control DNA sequence encoding a control protein having a detectable signal, and one or more 3' UTR sequence and one or more expression control sequence operatively associated with said control DNA sequence.

16. The assay system according to claim 15, wherein said DNA expression vector and said control DNA expression vector are provided in different stably transfected cell lines.

17. The assay system according to claim 15, wherein said DNA expression vector and said control DNA expression vector are provided in the same stably transfected cell line.

18. A high throughput method for screening libraries of compounds to identify compounds that affect the stability of mRNA comprising:

- (i) providing a stably transfected cell line comprising a DNA expression vector, which in the absence of a test compound is capable of expressing a protein having a detectable signal, wherein the mRNA which is transcribed from said expression vector and encodes said protein comprises at least one copy of a heterologous mRNA instability sequence;
- (ii) inoculating wells of one or more multi-well plates comprising a growth medium with said cell line;
- (iii)maintaining said one or more multi-well plates under conditions that allow cells of said cell line to grow and express said protein having a detectable signal;
- (iv)contacting the cells with one or more test compound;

(v) measuring said detectable signal; and

(vi) comparing the measured detectable signal with a control;

wherein a decrease in the measured detectable signal compared to said control indicates a compound that decreases mRNA stability and an increase in the measured detectable signal compared to said control indicates a compound that increases mRNA stability.

19. A kit comprising an assay system for screening for compounds which destabilize mRNA, said assay system comprising:

- (i) one or more DNA expression vector comprising a first DNA sequence encoding a protein having a detectable signal, one or more 3' UTR sequence and one or more expression control sequence operatively associated with said first DNA sequence, and a heterologous instability sequence DNA inserted into said 3' UTR sequence, said instability sequence DNA comprising a second DNA sequence corresponding to one or more mRNA instability sequence derived from one or more naturally occurring genes; and
- (ii) a control DNA expression vector comprising a control DNA sequence encoding a second protein having a detectable signal, one or more 3' UTR sequence and one or more expression control sequence operatively associated with said control DNA sequence; and optionally
- (iii) instructions for use.

20. The kit according to claim 19, further comprising one or more cell lines.

21. The kit according to claim 19, wherein said DNA expression vector and said control DNA expression vector are provided in different stably transfected cell lines.

22. The kit according to claim 19, wherein said DNA expression vector and said control DNA expression vector are provided in the same stably transfected cell lines.